REMARKS

Reconsideration of the allowability of the present application in view of the above amendments and the following remarks is requested respectfully.

Status of the Claims

Claims 1-3, 5, 7, and 19-41 were acted upon by the Examiner. Claim 19 has been canceled. Claims 1-3, 5, 7, 20, 21 and 26-41 have been rejected. Claims 22-25 have been deemed allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1 and 3 have been amended. Claims 1 and 3 have been amended to replace "amino acids 1-15 of SEQ ID NO:6" with "amino acids 25-39 of SEQ ID NO:11." Since the amino acid residues are identical, the amendment adds no new matter.

Summary of the Objections/Rejections

Claims 1-3, 20, 26, 28, 30, 32, 34, 36, 38, and 40 have been rejected under 35 U.S.C. § 112, first paragraph, as containing new matter. Claims 1-3, 5, 7, 20-21, and 26-41 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. There are no present novelty or obviousness rejections under 35 U.S.C. §§ 102, 103.

Summary of Examiner Interview

Applicants gratefully acknowledge the Examiner's interview with applicants' attorney, Marc Segal, on February 7, 2007. Applicants appreciate the Examiner's helpful suggestion with respect to Claim 1. During discussion of the new matter and written description rejections, applicants' attorney pointed to the disclosure in the specification that describes the claimed fusion constructs including the IL2 leader sequences, the soluble CD39 portions, and where the leader sequences are cleaved resulting in the sequences as recited in claims 1, 3, 5, and 7.

As a result of the interview, applicants undertook to amend claim 1 to make it clear that support for the claimed sequences are found in the specification as filed.

Discussion of New Matter Rejections

Claims 1-3, 20, 26, 28, 30, 32, 34, 36, 38, and 40 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner has indicated that this is a new matter rejection.

The Examiner asserts that the recitation "amino acids 1-15 of SEQ ID NO:6, amino acids 25-35 of SEQ ID NO:28, amino acids 27-34 of SEQ ID NO:29, and amino acids 21-24 of SEQ ID NO:30" in claims 1 and 3 represents a departure from the specification and the claims as originally filed and that applicant's citation to the specification does not provide support for this recitation. Applicants' traverse respectfully this rejection.

Claim 1 and 3 have been amended to replace "amino acids 1-15 of SEQ ID NO:6" with "amino acids 25-39 of SEQ ID NO:11." Although these are the exact same 15 amino acid residues, the sequence 25-39 of SEQ ID NO:11 is more clearly supported in the specification as discussed below.

Each of these particular sequences of amino acids is fused to a soluble portion of CD39 ("solCD39") in certain constructs identified and disclosed in the specification. During the expression of these fusion constructs in recombinant cells the N-terminal leader sequence is cleaved. It is the post-cleaved constructs that are isolated from the culture media and are tested in the assays described in the specification, and thus, it is the post-cleaved constructs that are used in applicants' claimed methods. The specification describes both the pre- and post-cleaved

amino acid sequences for the fused polypeptides by indicating the cleavage point in the amino acid sequence. Each one of these sequences is disclosed in the specification as being fused to a soluble portion of CD39 as follows:

- amino acids 25-39 of SEQ ID NO:11 (APTSSSTKKTQLTSS) – see page 39, line 6 (in the specification, the asterisk indicates the cleavage point and TQNK is the first four amino acids of solCD39);
- amino acids 25-35 of SEQ ID NO:28 (ASTKKTQLTSS) – see page 39, line 9 (in the specification, the asterisk indicates the cleavage point and TQNK is the first four amino acids of the fused solCD39);
- amino acids 27-34 of SEQ ID NO:29 (KKTQLTSS) – see page 39, line 11 (in the specification, the asterisk indicates the cleavage point and TQNK is the first four amino acids of the fused solCD39);
- amino acids 21-24 of SEQ ID NO:30 (APTS) – see page 40, line 13 (in the specification, the asterisk indicates the cleavage point and TQNKALPE is the first eight amino acids of the fused solCD39).

Because SEQ ID NOS. 11, 28, 29 and 30 contain the pre-cleaved amino acid sequences, it was necessary for applicants to recite only a portion of these sequences in the claims. Thus, each of these sequences is described in the specification as being fused to solCD39. Accordingly, this new matter rejection should be withdrawn.

The Examiner also asserts that the recitation "39-476 of SEQ ID NO:2" in claim 2 represents a departure from the specification and the claims as originally filed. This is clearly not new matter as this recitation is in claim 2 as originally filed. Accordingly, this new matter rejection should be withdrawn.

Discussion of Written Description Rejection

Claims 1-3, 5, 7, 20-21 26-41 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants traverse respectfully this rejection.

Claim 5 and its Dependent Claims

Applicants believe that based on the subject matter of claim 5, it is best to begin with a discussion of why claim 5 and its dependent claims are adequately described followed by a discussion of claims 1 and 3 and their dependent claims.

With respect to claim 5 and its dependents (claims 7, 21, 27, 29, 31, 33, 35, 37, 39, and 41), the Examiner asserts that the specification does not reasonably provide a written description of "any soluble CD39 polypeptide selected from the group consisting of amino acids 25-474 of SEQ ID NO: 28, amino acids of 27-473 of SEQ ID NO: 29 and amino acids 21-463 of SEQ ID NO: 30 for the claimed method of inhibiting platelet activation and recruitment." These claims, however, cover constructs that were *specifically disclosed* in the application.

In fact, each of the sequences recited in claim 5 are recited in original claim 6 (part a) as filed. Accordingly, there can be no question that these sequences are adequately described in the specification as filed. Moreover, the processing of each of these sequences is described in the specification as discussed below.

For example, the fusion construct that contains amino acids 25-474 of SEQ ID NO: 28 is disclosed in the specification at page 39, line 9 (the first 24 amino acids before the asterisk are cleaved from the construct). Moreover, the specification explains that the polypeptide encoded by this construct has "the sequence SEQ ID NO:28" and that "residues 36-474 are a soluble portion of CD39 and the predicted cleavage of the leader sequence is between Ser24 and Ala25." See page 39, lines 14-16. Accordingly, the post-cleaved sequence contains the amino acids 25-474 of SEQ ID NO: 28 as recited in claim 5.

Similarly, the fusion construct that contains amino acids 27-473 of SEQ ID NO: 29 is disclosed in the specification at page 39, line 11 (the first 26 amino acids before the asterisk are cleaved from the construct). Moreover, the specification explains that the polypeptide encoded by the this construct has the "sequence SEQ ID NO:29" and that "residues 35-473 are a soluble portion of CD39 and the predicted cleavage of the leader sequence is between Thr26 and Lys27." See page 39, lines 16-18. Accordingly, the post-cleaved sequence contains the amino acids 27-473 of SEQ ID NO: 29 as recited in claim 5.

Likewise, the fusion construct that contains amino acids 21-463 of SEQ ID NO: 30 is disclosed in the specification at page 40, line 13 (the first 20 amino acids before the asterisk are cleaved from the construct). Moreover, the specification explains that the polypeptide encoded by this construct has the "sequence SEQ ID NO:30" and that "residues 25-463 are a soluble portion of CD39 and the predicted cleavage of the leader sequence is between Gly20 and Ala21." See page 40, lines 16-18. Accordingly, the post-cleaved sequence contains the amino acids 21-463 of SEQ ID NO: 30 as recited in claims 5 and 7.

Although the Examiner has not objected to SEQ ID NO:6 and amino acids 25-464 of SEQ ID NO:27 recited in claim 5, these are similarly disclosed in the specification. The fusion construct SEQ ID NO:6 is disclosed on page 13, lines 18-21. The fusion construct that contains amino acids 25-464 of SEQ ID NO:27 is disclosed in the specification at page 38, lines 11-13. The specification explains that the polypeptide encoded by this construct has the "sequence of SEQ ID NO:27" and that "residues 26-464 are a soluble portion of CD39 and the cleavage of the leader sequence is between Ser24 and Ala25." Accordingly, the post-cleaved sequence contains the amino acids 25-464 of SEQ ID NO: 27 as recited in claim 5.

The Examiner asserts further that use of the term "has" is open-ended in claim 7 and that there is no disclosure regarding which amino acids may be added to the residues 21-463 of SEQ

ID NO:30. In response and without prejudice, applicants amended claim 7 in the previous Reply to state that "the soluble CD39 polypeptide *consists of* the sequence of amino acids 21-463 of SEQ ID NO: 30."

Moreover, the Examiner concedes that the specification discloses "a method for inhibiting platelet activation and recruitment by administering the specific soluble human CD39 [constructs] such as the ones disclosed at page 37-40 of the specification." As discussed above, claim 5 recites the sequences disclosed in original claim 6 and on pages 38-40 of the specification. These constructs are produced by recombinant cells and are cleaved prior to being secreted into the culture medium. Thus, the post-cleaved constructs are the sequences that would be used in any claimed method. As discussed in detail above, the specification describes both the pre- and post-cleaved sequences. Applicants have, thus, shown possession of the invention. See M.P.E.P. § 2163.02 ("An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997)."). Accordingly, this rejection should be withdrawn.

Claim 1 and its Dependent Claims

With respect to claim 1 and its dependents (claims 2-3, 20, 26, 28, 30, 32, 34, 36, 38, and 40), the Examiner asserts that the specification does not reasonably provide a written description of the full scope of claim 1.

Claim 1 is directed to a method for inhibiting platelet activation and recruitment in a mammal in need of such treatment comprising administering an effective amount of a soluble CD39 polypeptide consisting of a structure X-Y. Claim 1 as amended recites that X is defined as an Ala residue, amino acids 25-39 of SEQ ID NO:11, amino acids 25-35 of SEQ ID NO:28, amino acids 27-34 of SEQ ID NO:29, or amino acids 21-24 of SEQ ID NO:30. Y is defined as

(a) amino acids 36-478 of SEQ ID NO:2, (b) consecutive sequences of amino acids 36-478 of SEQ ID NO:2 with apyrase activity, (c) a variant polypeptide 95% identical in sequence to amino acids to (a) or (b); or (d) a polypeptide of (a), (b) or (c) with at least one conservative amino acid substitution.

Applicants have adequately described the X portion of the X-Y construct of claim 1 as discussed above – amino acids 25-39 of SEQ ID NO:11 (APTSSSTKKTQLTSS) is disclosed on page 39, line 6; amino acids 25-35 of SEQ ID NO:28 (ASTKKTQLTSS) is disclosed on page 39, line 9; amino acids 27-34 of SEQ ID NO:29 (KKTQLTSS) is disclosed on page 39, line 11; amino acids 21-24 of SEQ ID NO:30 (APTS) is disclosed on page 40, line 13.

With respect to subpart (a) of claim 1, these amino acids are simply the soluble portion of CD39 as disclosed in the specification at page 9, 6-9 ("Useful CD39 polypeptides include soluble forms of CD39 such as those having amino terminus selected from the group consisting of amino acids 36-44 of SEQ ID NO:2, and a carboxy terminus selected from the group consisting of amino acids 471-478 of SEQ ID NO:2."). Accordingly, the largest soluble CD39 portion consists of amino acids 36-478 of SEQ ID NO:2. Thus, the specification clearly disclose a polypeptide consisting of amino acids 36-478 of SEQ ID NO:2.

With respect to subparts (b), (c), and (d) of claim 1, applicants have adequately described the polypeptides within the scope of these subparts by providing the amino acid sequence in the sequence listing as filed (SEQ ID NO:2). The written description requirement does not require a description of the complete structure of every species within a chemical genus. *See Utter v. Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988). In *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324 (Fed. Cir. 2002), the Federal Circuit made clear that the written description requirement can be satisfied in a number of ways by disclosing, for example, "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some

combination of characteristics." Particularly relevant to this case, the Board of Patent Appeals and Interferences recently recognized that a claim drawn to a naturally occurring polypeptide that is at least 95% identical to a disclosed sequence is adequately described by the specification. *Ex parte Bandman*, Appeal No. 2004-2319 at p. 5 (BPAI 2005) (enclosed with prior Reply).

Here, applicants have provided the complete structure of SEQ ID. NO:2. Applicants have also disclosed the putative domain of soluble CD39 involved in apyrase activity. See Figure 2. Thus, with respect to subpart (b) one of skill in the art would be able to identify and verify, using the assays described in the specification, a consecutive amino acid sequence that has apyrase activity. With respect to subpart (c), applicants have provided guidance on page 10, lines 22-37 regarding how to select a polypeptide that is 95% identical to a given sequence. With respect to subpart (d), applicants have also provided on page 9, line 35 to page 10, line 4 of the specification a list of conservative amino acid substitutions. Moreover, such conservative substitutions were well-known in the art at the time this application was filed. Accordingly, applicants' disclosure of the structure in SEQ ID NO:2 coupled with the identity of the apyrase domain of CD39 and the assays to test apyrase activity is more than enough to adequately describe the polypeptides to one of skill in the art within the scope of claim 1.

Claim 3

With respect to claim 3, the Examiner asserts that the specification does not reasonably provide a written description of the full scope of claim 3.

Claim 3 is dependent upon claim 1 and, as amended, further defines X as (a) amino acids 25-39 of SEQ ID NO:11, amino acids 25-35 of SEQ ID NO:28, amino acids 27-34 of SEQ ID NO:29, and amino acids 21-24 of SEQ ID NO:30; (b) consecutive amino acids of such amino acids wherein the resulting X-Y polypeptide has apyrase activity; and (c) such amino acids with at least one conservative amino acid substitution wherein the resulting X-Y polypeptide has apyrase activity.

With respect to subpart (a), each of these sequences is specifically disclosed in the specification as discussed with respect to claim 1. With respect to subparts (b) and (c) of claim 3 and as discussed above, applicants have adequately described the polypeptides within the scope of these subparts by providing the amino acid sequence in the sequence listing as filed. One of skill in the art would be able to select consecutive amino acids from such sequences that when fused to soluble CD39 would retain apyrase activity. Moreover, using the guidance provided in the specification and the knowledge in the art at the time of filing, one of skill in the art would be able to identify conservative amino acid substitutions that would not destroy the apyrase activity of the fused polypeptide.

Accordingly, the written description rejections should be withdrawn.

Disclosure of Related Application

Applicants note that a related application, U.S. Application No. 09/835,147 (the '147 application) was filed on April 13, 2001 as a continuation-in-part of International Application No. PCT/US99/22955 and which claims the benefit of the same provisional applications as the present application. The '147 application has been abandoned. Applicants note that Examiner Huyhn was the Examiner of record for the '147 application. Although applicants do not believe that it is required, applicants request that the Examiner advise the undersigned if applicants should identify the '147 application in an Information Disclosure Statement. If so, applicants request that the Examiner advise applicants prior to the issuance of a Notice of Allowance or other action.

Conclusion

In view of the proposed claim amendment and the arguments presented above, the present application is believed to be in condition for allowance and an early notice thereof is

earnestly solicited. Applicants request that the Examiner contact the undersigned if any issues remain.

Respectfully submitted,

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